**IN THE UNITED STATES DISTRICT COURT**
**FOR THE DISTRICT OF DELAWARE**

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| BIOVAIL LABORATORIES INTERNATIONAL SRL a corporation of Barbados, | ) | |
| Plaintiff, | ) | C.A. No. 05-586-GMS |
| | ) | C.A. No. 05-730-GMS |
| v. | ) | C.A. No. 06-620-GMS |
| | ) | CONSOLIDATED |
| ANDRX PHARMACEUTICALS, LLC and ANDRX CORPORATION | ) | **PUBLIC VERSION** |
| Defendants. | ) | |

**DEFENDANTS' ANSWERING BRIEF**
**ON CLAIM CONSTRUCTION**

OF COUNSEL:

Steven Maddox
Jeremy J. Edwards
FOLEY & LARDNER, LLP
3000 K Street, N.W., Suite 500
Washington, DC 20007
Tel: (202) 672-5300

Douglas Carsten
FOLEY & LARDNER, LLP
11250 El Camino Real, Suite 200
San Diego, California 92130
Tel: (858) 847-6700

Martin P. Endres
HEDMAN & COSTIGAN, P.C.
1185 Avenue of the Americas
New York, New York 10036
Tel: (212) 682-7474

Richard L. Horwitz (#2246)
Kenneth L. Dorsney (#3726)
POTTER ANDERSON & CORROON LLP
Hercules Plaza, 6th Floor
1313 N. Market Street
Wilmington, DE 19899
Tel: (302) 984-6000
Fax: (302) 658-1192
rhorwitz@potteranderson.com
kdorsney@potteranderson.com

*Attorneys for Defendants Andrx Pharmaceuticals, LLC and Andrx Corporation*

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## I. INTRODUCTION

Looking beyond the rhetoric pervading Biovail's opening brief, Andrx demonstrates in what follows why, as a matter of law, the Court should reject Biovail's construction of the disputed claims.

The keystone to Biovail's primary arguments is extrinsic evidence in the form of a declaration from Dr. Brenner. Biovail simply could not make its case on the patent and the prosecution history as written, and as available to the public. Accordingly, Biovail brought Dr. Brenner in to testify to a wide variety of alleged aspects of the invention that are nowhere to be found in the patent, and to testify as to what the inventors meant to say to the PTO that again is nowhere to be found in the prosecution history. Thus, Biovail suggests that the public could not possibly have known what the patent meant unless it hired Dr. Brenner (a) to say what the inventors meant to say, *instead of what the inventors did say*, and (b) to say what the invention was about, *instead of what the patent said the invention was about*.

In what follows, Andrx demonstrates that the rest of Biovail's contentions likewise run contrary to well-settled principles of claim construction.

## II. ARGUMENT

### A. THE '791 PATENT

The '791 patent is the one that Biovail already litigated and lost against Andrx, and specifically the same diltiazem beads that comprise Andrx's accused product in this case. *See Biovail Corp. v. Andrx Pharmaceuticals, Inc.*, 158 F. Supp. 2d 1318 (S.D. Fla. 2000), *aff'd*, 239 F.3d 1297 (Fed. Cir. 2001) (hereinafter, "*Biovail I*"). Biovail now asks this Court to second-guess both the careful analysis of intrinsic evidence performed by the district court in Florida, and even the portion of that claim construction that the Federal Circuit expressly adopted in affirming dismissal of Biovail's case.

### 1. The Limitation "extended-release galenical composition" Refers to the Pre-Ingestion Dry State.

The district court in *Biovail I* squarely rejected Biovail's attempt to construe the claimed pharmaceutical composition of the '791 patent to refer to whatever interactions in the gastro-intestinal fluid might occur after the claimed composition is ingested. In a lengthy opinion after a five-day bench trial, the district court found that the intrinsic evidence of the specification and prosecution history (the same intrinsic evidence again proffered by Andrx in this case) supported construing the claims to refer to the pharmaceutical composition as manufactured and sold – and not to whatever may happen to that composition after ingestion. *Biovail I*, 158 F. Supp. 2d at 1321-1323.

The Florida district court's hard work and thoughtful analysis of the intrinsic evidence should be given the kind of careful consideration that this Court would expect from another court asked to construe a patent that this Court previously had construed. After all, the controlling intrinsic evidence has not changed between *Biovail I* and this case. The only possible difference in the evidentiary record this time would be the extrinsic evidence of Dr. Brenner's declaration.

Further, in giving the *Biovail I* court's claim construction the careful consideration warranted, this Court also should bear in mind that the out-of-body construction in *Biovail I* is consistent with several courts' constructions of similar pharmaceutical claims, including a decision from this District, which the Federal Circuit affirmed. *Novartis Pharmaceuticals Corp. v. Eon Labs*, 234 F. Supp. 2d 464 (D. Del. 2002) (Farnan, J.), *aff'd*, 363 F.3d 1306 (Fed. Cir. 2004). In *Novartis*, this District and the Federal Circuit held that claims to the compound "hydrosol" were limited to "medicinal products prepared outside of the body", as opposed to "products formed within the stomach of a patient after a particular medicinal product has been ingested." *Id.*, 363 F.3d at 1308-1311. The Federal Circuit based this construction on the intrinsic evidence of the specification and prosecution history (the same type of evidence offered by Andrx and ignored by Biovail in this case), and on the same basis distinguished the *Zenith*

case cited by Biovail in this case. *Id.*, at 1311; *see* Biovail Br. at 18 (citing *Zenith Labs, Inc. v. Bristol-Myers Squibb Co.*, 19 F.3d 1418 (Fed. Cir. 1994)).

More recently, the United States District Court for the District of New Jersey – which has perhaps the largest docket of pharmaceutical patent cases in the country – likewise rejected a similar attempt by a Hatch Waxman Act plaintiff to construe claims to a "pharmaceutical composition" to include whatever occurred after ingestion and introduction into the gastro-intestinal tract. *Ortho-McNeil Pharmaceutical v. Kali Laboratories*, No. 02-5707 (JCL), 2007 U.S. Dist. LEXIS 25459 (D.N.J. April 4, 2007) (Exhibit A hereto). Again, the court relied on the intrinsic evidence of the specification and prosecution history, which, as here, reflected that the invention was a manufactured medicinal preparation or dosage unit, and not some process or interaction that allegedly occurs inside the body. *Id.* at *40-43.

And yet again, in *Marion Merrell Dow Inc. v. Baker Norton Pharmaceuticals*, 948 F. Supp. 1050 (S.D. Fla. 1996), the court rejected a Hatch Waxman Act plaintiff's attempt to assert that a claimed "compound" should be construed against the intrinsic evidence to cover the compound as allegedly created inside the body by metabolic processes that acted upon the accused product, as well as the usual manufacture of medicinal preparations. The *Marion* court found that the structure of the claims, the specification, and the prosecution history all indicated that the invention concerned the manufacture of pharmaceutical preparations, as opposed to whatever processes acted upon a product. *Id.* at 1053-1055. The court also expressly rejected the same *Zenith* argument made by Biovail in this case: "The Court declines to find a *per se* rule in *Zenith* which requires that all claims which describe a compound be construed as covering both the metabolically produced and synthetic produced forms of the compound, without regard to the language of the claims, the specification of the patent or the prosecution history." *Id.* at 1054 n.4.

Indeed, the present case is even more compelling than *Novartis* and *Marion*, where the claimed invention was a chemical compound – that is, a pharmaceutically active ingredient. Here, as in *Ortho-McNeil*, the claimed invention is a "galenical (or pharmaceutical)

composition," which includes an active ingredient in a particular form, in a particular admixture with another ingredient, and with a particular coating. The difference is substantial. An argument can be made in some cases, such as *Zenith*, that a claim to a compound may be read to include the compound regardless of whether it is created outside of the body or inside. After all, the human metabolic processes involve the synthesis of compounds. However, Andrx is unaware of, and Biovail does not cite, any cases in which a court has held that a "pharmaceutical composition" can be formed in the body. Metabolic processes do not include the creation of compounds in specific beads, in a specific admixture, and with a specific coating.

As against the same specification and prosecution history cited by the district court in *Biovail I* and by Andrx in its opening brief, Biovail offers a fragment from the language in claim 1: "pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein. . . ." (Joint Appendix of Intrinsic and Extrinsic Evidence (hereinafter "J.A.") Tab 1, A-7 – A-8 at 8:67 – 9:2.) As a matter of law, Biovail fails to cite any authority for the proposition that such a snippet would be sufficient to warrant construing the claim to cover not only what anyone does in manufacturing the dosage form, but also whatever processes occur and interact with the dosage form after being ingested. As a matter of fact, the clause clearly recites that the composition that constitutes the invention ***will meet*** the pH of the gastrointestinal tract sometime in the ***future***.

The intrinsic evidence is clear that the inventors did not believe that their invention included the composition in the wet state. The inventors went out of their way, repeatedly, during the prosecution history to emphasize the importance of manufacturing beads containing diltiazem salt and wetting agent homogeneously ***in the dry state***.

> Furthermore, by the very nature of the process by which the present beads are made, the beads produced are homogeneous. Their homogeneity arises from the extrusion-spheronization process by which they are made.

(J.A. Tab 2, A-16 (emphasis in original).)

> Thus, at the outset, it is noted that the present composition is characterized by the use of beads consisting essentially of in admixture together an effective amount of Diltiazem or one of more salts thereof as an active ingredient and the wetting agent as defined in the claim. The beads are also coated with a microporous membrane as defined in the claims.

(J.A. Tab 5, A-71 (emphasis in original.)

> [E]ach of the independent claims has a separate reference therein to a coating, making it clear that the "beads" are apart from the coating and, in fact, have a coating thereon. Thus, the reference to "beads" is to uncoated beads.

(J.A. Tab 4, A-62-63 (emphasis in original).)

> In fact, such a procedure is impossible as microgranules of the type constituted by a central core as in Debregeas et al cannot be produced by the extrusion-spheronization process. By contrast, in accordance with the present invention, the extrusion-spheronization process leads to homogeneous type beads while the "building-up" process, starting with a sugar core, leads to heterogeneous type beads. Clearly, it is impossible to have a sugar central core in a homogeneous bead as in the present invention. Such a bead is, by nature, heterogeneous.

(J.A. Tab 5, A-74 (emphasis in original).)

Biovail further accuses Andrx's construction of "ignor[ing] the purpose of the invention." (Biovail Br. at 19.) It is well-settled, however, that the claims are to be construed as they are written, and the "purpose" of the invention is not to be read into the claims as a claim limitation. *See Storage Tech. Corp. v. Cisco Sys., Inc.*, 329 F.3d 823, 831 (Fed. Cir. 2003) (holding that the district court erred in reading limitations into the claims from the purpose of the invention); *Ampex Corp. v. Eastman Kodak Co.*, 460 F. Supp. 2d 541 (D. Del. 2006) (refusing to read a limitation into the claims without any support in the claim language); *Kimberly-Clark Corp. v. Tyco Healthcare Retail Group*, 456 F. Supp. 2d 998, 1012 (E.D. Wis. 2006) (rejecting Tyco's attempt to limit the claim, because "Tyco's only support for the limitation is found in the general purpose of the invention . . . [but t]he patent itself teaches none of these properties"). If this were not the law, all patentees would follow Biovail's lead of submitting extrinsic evidence (in this case, the Brenner Declaration) of what the patentees now claim the "purpose" of the invention

was for purposes of the litigation, and simply declare that the claims must be construed to fulfill that litigation-inspired "purpose."

Biovail complains that under Andrx's construction, "pharmaceutical compositions that are not dry, such as liquid filled capsules, injectables and syrups, are not even galenical or pharmaceutical compositions." (Biovail Br. at 19.) Andrx made no such assertion. Indeed, Andrx specifically stated in its Opening Brief that galenical compositions were known "to refer to compositions that were designed to be used in or on the body to achieve a pharmacological result." (Andrx Br. at 6.) However, simply because a particular composition was ***designed to be used*** in the body does not mean that a composition claim written as claim 1 of the '791 patent ***covers the actual use*** of that composition within the body. After all, every pharmaceutical composition, including the one in *Ortho-McNeil*, is intended to be used in the body.

The principles of claim construction cited by Biovail actually support Andrx's position. Biovail cites to *Rexnord Corp. v. Laitram Corp.*, 274 F.3d 1336, 1342 (Fed. Cir. 2001), for the proposition that "a claim term should be construed consistently with its appearance in other places in the same claim or in other claims in the same patent." (Biovail Br. at 11, 20.) This legal principle in fact supports Andrx's view that the composition must be read to refer only to the dry state. As Andrx cited in its opening brief, dependent claim 3 of the '791 patent clearly refers to "the composition of claim 1" and further states that the amount of wetting agent must be "about 8% by weight of the composition." If the claims were read to include the post-ingestion, wet state, as Biovail contends, it would be impossible to know whether the composition contained "about 8% by weight of the composition" because an unknown amount of gastric fluid would enter the composition, adding an unknown amount of weight to the composition. Thus, application of the *Rexnord* principle establishes that the composition is properly construed to refer to the dry state.

### 2. The Limitation "beads" Refers to the Dry, Uncoated Material That is Coated With a Microporous Membrane.

With respect to the claimed "beads," Biovail purports to rely on the "plain language" of Claim 1, but ultimately resorts to the unsupported (and faulty) premise that because the "beads" are intended to be ingested at a later time, the inventors must have claimed any structure having a wetting agent and a diltiazem salt in admixture. (Biovail Br. at 20.) From this faulty premise, Biovail simply pronounces, *ipse dixit*, that a construction of "beads" that is limited to the dry state is (a) "[w]ithout any support whatsoever" and (b) would render claim 1 "meaningless." (Biovail Br. at 21.)

This is simply not so, and Biovail's construction is unsound for a host of reasons. First, as an initial matter, Biovail's interpretation of the "plain meaning" of the claim language is neither dispositive nor persuasive. As explained above, the mere fact that the claimed beads are intended for ingestion does not mean the inventors necessarily claimed "beads" that might form after ingestion. Indeed, the claim language is temporally forward-looking, indicating that the claimed composition comprising beads "***will meet***" adverse conditions after ingestion. (J.A. Tab 1, A-8 at 9:1.) At the very least, this suggests a conceptual rift between the "beads" that were claimed, and what they may form later *in vivo*. *See supra* at 6-8.

Second, as demonstrated in its opening brief, Andrx's construction finds ample support throughout the intrinsic record; the inventors consistently referred to "beads" in their dry state, and not in their wet state. (*See* Andrx Br. at 8-10 (citing both specification and prosecution history).) Ironically, it is ***Biovail*** that fails to cite even a single page of specification or prosecution history in support of its construction of "beads." (*See* Biovail Br. at 20-21.)

Third, the inventors' express definition of "beads" strongly suggests that they only claimed "beads" formed in the dry state. Indeed, to overcome a rejection, the applicants explained that

> each of the independent claims has a separate reference therein to a coating, making it clear that the "beads" are apart from the coating and, in fact, have a coating thereon. Thus, the reference to "beads" is to uncoated beads.

(J.A. Tab 4, A-62-63 (emphasis in original).) Because the claimed "beads" are uncoated, they cannot be wet and still make any sense in the context of the specification. The specification describes the beads as "spherules" with a measurable diameter. (*See* J.A. Tab 1, A-5 at 3:10-12; 4: 48-52 ("beads are presented in form of spherules the diameter of which is between about 0.05 mm and 3 mm . . .") ("beads are dried . . . [and] calibrated to the necessary diameter").) But wet, uncoated "beads" would be *amorphous* solutions of dissolved diltiazem salt, wetting agent, and solvent. They would not be spherules or have any measurable diameter. Further, nothing in the specification suggests that the described coating methods ("pulverization" and "spray gunning") can be used to coat an amorphous, uncoated, wet "bead." These methods are only described as coating dry "beads." (J.A. Tab 1, A-5 – A-6 at 4:64 – 5:3.)

Accordingly, the Court should construe "beads" to refer to the dry, uncoated material that is subsequently coated.

### 3. The Limitation "each bead" Refers to Every Single Bead.

Biovail argues that "each bead" can refer only to its antecedent in the claim ("beads containing an effective amount of . . . Diltiazem salts as the active ingredient"). (Biovail Br. at 21-22.)[1]

In effect, Biovail is asking the Court to rewrite claim 1 to replace the phrase "each bead" with the phrase "said beads." But if the inventors wanted to use the phrase "said beads" to

[1] As predicted, Biovail also attempts to argue that because claim 1 is open-ended, the claimed formulation may include "cushioning beads to help preserve the integrity of the beads when compressing them into tablets." (Biovail Br. at 21.) This is simply irrelevant. First, the '791 patent specification and the intrinsic evidence make no reference to these new, mysterious "cushioning beads" – giving rise to evident written description and enablement issues if so construed. *See* 35 U.S.C. § 112. Indeed, the '791 patent specification and intrinsic record are clear that beads used in the composition are an admixture of diltiazem salt and wetting agent. (*See, e.g.*, J.A. Tab 1, A-4 at 2:54-58; A-5 at 4:48-49, 4:64-67; Tab 5, A-71 – A-72.) Second, Andrx has already demonstrated that even in open-ended claims the word "each" can refer to "every single one." (Andrx Br. at 12-13.) It is apparent that Biovail is seeking through construction to allow after-the-fact selection of some diltiazem-containing beads to argue infringement. This is improper, and eliminates the requirement of "each" bead.

merely refer to an antecedent, they would have. Indeed, later in Claim 1, and throughout the specification, ***they did***. (*See* J.A. Tab 1, A-5 at 4:50, 64, 67; and A-8 at 9:2.) Biovail cannot play mix-and-match with different claim terms to avoid their plain meaning. As explained in Andrx's opening brief, the plain meaning of "each bead," consistent with use of the word "each" in the specification and prosecution history, require that every single bead must contain diltiazem salt and wetting agent in admixture. (Andrx Br. at 11-14.) Accordingly, the Court should adopt Andrx's construction of "each bead."

**4. The Limitation "an effective amount of wetting agent" Requires That the Wetting Agent Actually Act Within the Bead.**

Biovail asserts that "[n]othing in the language of Claim 1 states or suggests that the wetting agent only serves its purpose within the beads." (Biovail Br. at 22.) But the requirement that the wetting agent act within each bead is right there in Claim 1, plain as day. Claim 1 states, "each bead containing one or more of the Diltiazem salts and an effective amount of wetting agent in admixture with the one or more Diltiazem salts ***to maintain the solubility of the Diltiazem in each bead*** . . . ." (J.A. Tab 1, A-7 at 8:62-66 (emphasis added).)

As Andrx explained in its opening brief, the intrinsic evidence confirms that the claims require that the wetting agent act within the bead to maintain the solubility of the Diltiazem. (Andrx Br. at 13-14.) First, the claim language requires it by its very words. (J.A. Tab 1, A-7 at 8:62-66.) Second, the inventors confirmed that the wetting agent must act within the bead to control the solubility of diltiazem. The inventors represented to the patent office that "the wetting agent appears to ***control or strongly influence*** the solubility of the Diltiazem . . . . [And t]his control appears to ***occur within the core*** of Diltiazem and wetting agent." (J.A. Tab 5, A-71 (emphasis added); see also J.A. Tab 5, A-77 ("the wetting agents claimed in the present invention are substances which are believed to modify the solubility of Diltiazem ***inside the coated beads*** . . ." (emphasis added).)

For these reasons, the Court should adopt Andrx's proposed construction of the term "an effective amount of wetting agent."

### 5. The Limitation "admixture" Requires Homogeneity in the Dry State.

Yet again, Biovail seeks to confuse the issue of what a particular composition was designed to do with what a particular patent claim actually covers. Even worse, Biovail is attempting to broaden the claim scope beyond what the '791 patent disclosure supports. The specification describes a complete composition with specific physical attributes and qualities in a dry state before ingestion. (J.A. Tab 1, A-3-7.) No suggestion or teaching exists in the intrinsic record of this patent to support a deviation from this disclosure. Yet Biovail's proposed construction of "admixture" attempts to encompass an "admixture" that occurs only during digestion. Such a construction is at odds with the intrinsic evidence. Andrx's proposed construction that admixture refers to homogeneous diltiazem salt and wetting agent[2] in each beads in their dry state is correct.

Biovail's limited reliance on the '791 specification disclosure misses the mark. Biovail cites a handful of lines and two figures in the '791 patent specification which refer to desired bioavailability and smooth drug-release profiles. (Biovail Br. at 14.) Biovail concludes from this evidence that "only if the wetting agent performs its function *in vivo* can the disclosed benefits of the claimed formulations be realized." (*Id.*) Significantly, however, the inventors of the '791 patent chose not to include in their claims any particular release-profile limitations or bioavailability limitations. (*Compare* J.A. Tab 1 A-7 – A-8 at 8:59 – 10:11 (claims as allowed without release profile limitation) *with* J.A. Tab 2 A-13 – A-14 (pending claim 27 including

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[2] Biovail also makes the astonishing statement that "the concept of a wetting agent in the dry state is nonsensical." (Biovail Br. at 13.) The '791 patent expressly defines "wetting agent" through a laundry list of materials in claim 1. (J.A. Tab 1, A-8 at 9:7 – 13.) The claims of the '791 patent do not distinguish between "dry" or "wet" wetting agents. *Id.* Biovail itself agreed to a definition of wetting agents in this very litigation that did not differentiate between "dry" and "wet" wetting agents. (Jt. Claim Chart at Ex. A.) Moreover, the '791 patent specification describes forming dried beads containing "wetting agents" that are in the dry state. (J.A. Tab 1, A-6 at 5:54 – 6:23.) Similarly, the prosecution history contains numerous passages referencing wetting agents in "dry" form (*e.g.*, J.A. Tab 2, A-25; Tab 4, A-53), and one of the inventors filed a declaration in which he described formulating homogeneous beads containing a "wetting agent." (J.A. Tab 3, A-28.) If the concept of a dry wetting agent is "nonsensical," then Biovail need look no further than its own doorstep to find nonsense.

release-profile limitation).) Consequently, these statements are not related to the '791 patent's ***claim limitations***. Further, just because the wetting agent must be in admixture *in vivo* to maintain the solubility of Diltiazem does not necessarily mean that the inventors claimed a wet admixture. As explained below, the inventors' own statements during prosecution suggest that they did not.

Biovail's resort to the file history is similarly unavailing. Biovail contends that a passage from a June 22, 1992 Amendment supports their construction. (Biovail Br. at 15 (quoting J.A. Tab 2, A-21).) Biovail characterizes the excerpt as follows: "The inventors explained to the Patent Office that the sugar in the core of Debregeas cannot act as a wetting agent because the Debregeas formulations do not provide an opportunity for the sugar to form a ***homogeneous admixture*** with diltiazem hydrochloride." (Biovail Br. at 15 (emphasis added).) Biovail fails to inform the Court that the word "admixture" did not appear in the original specification as filed, and had ***not even yet been added*** to any pending claim when that amendment was filed. (J.A. Tab 2, A-10 – A-14 (then-pending claims, none of which contain admixture limitation).) Thus, the quoted portion of the prosecution history does ***not*** use the term "admixture," does ***not*** refer to the word "admixture" in the specification (because the specification does not contain the word admixture), and does ***not*** refer to any "admixture" claim limitation (because the word had not yet been added to any pending claims). Given these facts, it is clear that the inventors were ***not*** discussing the admixture limitation in that Amendment.

Moreover, as Andrx explains in its opening brief, this passage distinguishes a particular piece of prior art, the Debregeas reference, in which diltiazem is applied to a central sugar core. The sugar core structure of Debregeas is the same sugar core structure used in Andrx's proposed product. The quoted passage from the prosecution history essentially concludes that even when wet, the sugar in the core ***cannot*** act as a wetting agent in a bead manufactured in such a manner. Biovail has a problem: the inventors distinguished their claimed invention from the prior art based on [redacted] Biovail cannot capture after issuance the prior art structure it distinguished during prosecution.

Biovail tries to get out from under this disastrous prosecution history by having Dr. Brenner rewrite the prosecution history in his declaration. In what can most charitably be called a desperate rescue effort, Dr. Brenner declares that the inventors did not mean what they said - - but rather, that the admixture simply cannot form in the Debregeas reference ***bead***. Dr. Brenner concocts an after-the-fact cover story in which the Debregeas reference contains a coating which must first "rupture," followed by dissolution of all the diltiazem, followed then again by dissolution of the sugar core. (Biovail Br. at 15 (citing Decl. of Gerald S. Brenner Ph.D. in Support of Biovail's Opening Claim Construction Br. (D.I.148) ("Brenner Decl.")).)

The most fundamental problem with Biovail's rescue effort is that, as a matter of law, it does not matter what the inventors "meant" or "could" have told the PTO about Debregeas. The public is entitled to rely on what the inventors actually told the PTO. *See Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576 (Fed. Cir. 1996) ("The claims, specification, and file history, rather than extrinsic evidence, constitute the public record of the patentee's claim, a record on which the public is entitled to rely. In other words, competitors are entitled to review the public record, apply the established rules of claim construction, ascertain the scope of the patentee's claimed invention and, thus, design around the claimed invention); *Bayer Healthcare LLC v. Abbott Labs.*, C.A. No. 03-189-GMS, 2005 U.S. Dist. LEXIS 21042, at *13-14 (D. Del. Sept. 26, 2005) (Sleet, J.) (Exhibit B hereto) ("the prosecution history of a patent serves an important public-notice function because it is a written record of both the inventor's understanding of the invention, and the limitations the inventor may have placed on the invention in order to distinguish it from prior art . . . As a basic principle of claim interpretation, prosecution disclaimer promotes the public notice function of the intrinsic evidence and protects the public's reliance on definitive statements made during prosecution.").

In fact, the inventors ***never*** told the patent office that the coating of the Debregeas reference would rupture or disrupt, nor did the inventors ***ever*** attribute the failure of the Debregeas bead to contain an admixture to the particular coating disclosed in the Debregeas reference at all. Instead, the inventors clearly stated, repeatedly, that the failure of the Debregeas

reference bead to contain a homogeneous mixture of diltiazem salt and wetting agent had to do with the method of manufacturing the ***dry bead***.

> Furthermore, by the very nature of the process by which the present beads are made, the ***beads produced are homogeneous***. Their homogeneity arises from the extrusion-spheronization process by which they are made.

(J.A. Tab 2, A-16 (emphasis added).)

> Further, the galenical Diltiazem preparation described by Debregeas et al clearly does not disclose a Diltiazem bead composition containing a wetting agent, prepared by the extrusion spheronization process. Such a bead composition is necessarily a homogeneous bead composition. By contrast, the "building-up" process described by Debregeas et al is of no utility for the present invention as the present invention does not use the "building-up" process.

(J.A. Tab 2, A-18 (emphasis in original).)

> In order to demonstrate the "center" or "core" of the present pharmaceutical composition is an inherently homogeneous or uniform composition of Diltiazem or one or more salts thereof and wetting agent, the following experiment was conducted.

(J.A. Tab 3, A-28.)

> This step was carefully evaluated, as can be seen by the amount of analyses performed, as it is essential to the performance of the final product that the components of the core be homogeneously mixed.

(J.A. Tab 3, A-30 – A-31.)

> Thus, at the outset, it is noted that the present composition is characterized by the use of beads consisting essentially of in admixture together an effective amount of Diltiazem or one or more salts thereof as an active ingredient and the wetting agent as defined in the claims.

(J.A. Tab 4, A-50 (emphasis in original).)

> In particular from column 3, lines 3-31, of Debregeas et al, it is clear that the process thereof results in a compositional form having i) a 'core' of mutual [sic] excipient, which is described as a mixture of saccharose or fructose and starch, ii) an outer layer thereon of polyvinylpyrrolidone (PVP) and Diltiazem and iii) a

> coating thereon. Thus, in Debregeas et al, Diltiazem is in admixture with only PVP, and not with the 'core' or that composition.
>
> By contrast, the present formulation contains Diltiazem or one or more salts of thereof in admixture together with the wetting agent.

(J.A. Tab 4, A-51 (emphasis in original).)

> In fact, such a procedure is impossible as microgranules of the type constituted by a central core as in Debregeas et al cannot be produced by the extrusion-spheronization process. By contrast, in accordance with the present invention, the extrusion-spheronization process leads to homogeneous type beads while the "building-up" process, starting with a sugar core, leads to heterogeneous type beads. Clearly, it is impossible to have a sugar central core in a homogeneous bead as in the present invention. Such a bead is, by nature, heterogeneous.

(J.A. Tab 4, A-53 – A-54 (emphasis in original).)

> In summary, inasmuch as both cited references prepare a product by a method different from the present invention, and inasmuch as these processes are incompatible with the present process and further inasmuch as the present product is distinguishable in at least one property over that of Debregeas et al, it is believed that each claimed aspect of the present invention is fully patentable over the cited references.

(J.A. Tab 5, A-82 (emphasis in original).)

In addition to being wholly divorced from any statements the public could find in the prosecution history, Dr. Brenner's analysis is inconsistent with the Debregeas reference. First, Debregeas describes a slow-release preparation of Dilitiazem, but the sort of membrane rupture referred to by Dr. Brenner would result in a "dose dump" associated with a quick release composition. (J.A. Tab 25, A-907.) (Decl. of Professor Roland Bodmeier, Ph.D. in Support of Andrx's Answering Claim Construction Br.) at ¶ 30. Second, Dr. Brenner's analysis is incomplete, because it apparently focuses on only one embodiment in Debregeas. *Id.* at ¶¶ 31-32. Third, although Debregeas describes more than one coating, Dr. Brenner refers only to one such coating as a way to further distinguish the claimed invention of the '791 patent from Debregeas. *Id.* at ¶ 33. But another coating described in Debregeas is within the scope of

Claim 1 of the '791 patent. *Id.* Thus, Dr. Brenner's analysis of the prosecution history with respect to Debregeas is inherently flawed.

Biovail's remaining citations to the file history are similarly unpersuasive, and ignore the inventors' repeated emphasis on the importance of the manner in which the invention was prepared in the dry state. These citations simply refer to the fact that the critical claimed wetting agent must maintain the solubility of the diltiazem when the composition is actually used, *i.e.*, ingested. The claims of the '791 patent, however, are not method of use claims, nor do they include dissolution or bioavailability limitations. Consequently, the passages Biovail cites do not undermine Andrx's well-supported construction requiring the claimed ***admixture*** to be formed in the dry composition.

Finally, Biovail tries to reverse the Federal Circuit by disregarding the plain meaning "homogeneous." Federal Circuit has previously construed this limitation to require that the bead containing the admixture be homogeneous – the construction that Andrx is proposing here:

> The prosecution history of the '396 application clearly indicates that at least the "***bead***" described in the '396 application, in claims 1, 6, and 11 of the '505 patent, and in claim 1 of the '791 patent must be "***homogeneous***." Claim 1 of the '791 patent provides that the "***bead***" contains a diltiazem salt and a wetting agent in "***admixture***." Therefore, the ***admixture of diltiazem salt and wetting agent that comprises the bead of claim 1 of the '791 patent must be homogeneous***.

*Biovail Corp. International v. Andrx Pharmaceuticals, Inc.*, 239 F.3d 1297, 1302 (Fed. Cir. 2001) (emphasis added).

Biovail would read the concept of uniformity out of the word "homogeneous." (Biovail Br. at 18-19.) However, the dictionary definition relied upon by Biovail unambiguously states that homogeneous means "uniform in structure or composition throughout." (J.A. Tab 7, A-95.) Similarly, Andrx's dictionary definition similarly provides that homogeneous means "composed of parts all of the same kind," or "of the same kind or nature; essentially alike." (J.A. Tab 9, A-101.) Biovail sniffs that these definitions do not use the word "identical," which appears in

Andrx's proposed construction. This is a distinction without a difference. The previous District Court decision against Biovail expressly construed the word "homogeneous" to mean "samples of the product taken anywhere throughout the product should have the same composition." *Biovail Corp. International v. Andrx Pharmaceuticals, Inc.*, 158 F. Supp. 2d 1318, 1325 (S.D. Fla. 2000). While the Federal Circuit did not adopt any particular construction of "homogeneous," the Federal Circuit did expressly state that the District Court construed "admixture" consistently with the Federal Circuit's construction. *Biovail I*, 239 F.3d at 1303. Thus, despite Biovail's attempts to read "homogeneity" out of the construction, the Court should require that homogeneous mean homogeneous by requiring that the composition of the bead be uniform, *i.e.*, identical, at all locations throughout the bead.

For all of these reasons, the Court should construe the term "admixture" in accordance with Andrx's proposed construction.

**6. The Limitation "to maintain the solubility of the Diltiazem in each bead" Requires That the Wetting Agent Actually Act in the Bead to Keep the Solubility Value of Diltiazem Constant.**

Biovail seeks to eliminate the requirement that the critical wetting agent component of the composition have any function whatsoever in the composition. The inventors were clear throughout the prosecution of the '791 patent that the wetting agent had to ***act*** affirmatively to control the solubility of the diltiazem in the bead.

> In essence, in admixture, the wetting agent appears to control, or strongly influence, the solubility of Diltiazem and does not permit this solubility to be affected by pH or other adverse conditions in the gastrointestinal tract. Further, this control appears to occur within the core of Diltiazem and wetting agent. This control affords a gradual release of Diltiazem in a relatively uniform manner over a period of about 24 hours.

(J.A. Tab 5, A-71.) The inventors repeatedly distinguished prior art based on the presence of a homogeneous admixture containing a wetting agent in the dry state. (*See, e.g.*, J.A. Tab 5, A-71 – A-72, A-74, A-79, A-82.)

Now, however, Biovail seeks to denigrate the role of the critical wetting agent. Instead of requiring the wetting agent to actually ***do*** anything, Biovail proposes a construction in which the wetting agent need only not "prevent a gradual release of the drug in a relatively uniform manner." (Biovail Br. at 23.) In essence, Biovail reads the limitation "maintain the solubility" to require merely that the wetting agent not do anything to interfere with the release of diltiazem from the composition.

Biovail's proposal is at odds with the claim language, the intrinsic evidence, and the extrinsic evidence Biovail proffers. The claim language requires that the wetting agent act to maintain the ***solubility*** of the diltiazem in each bead – not that the wetting agent merely not interfere with the ***release*** of diltiazem from the composition. (J.A. Tab 1, A-7 at 8:64-66.) As Biovail's expert witness, Dr. Brenner, testifies, solubilization is a different process than release. (Brenner Decl., ¶¶ 10-13 (identifying three distinct stages in membrane-based oral dosage forms – (1) solubilization, (2) transport across the membrane (*i.e.*, release), and (3) absorption into the body.) Biovail now seeks to read the limitation to refer actually to ***release***, and not solubility. As such, Biovail's proposed construction is belied by the plain language of the claim itself. (Bodmeier Decl. at ¶ 21.)

The reason for Biovail's construction, of course, is clear: one cannot tell *in vivo* whether the wetting agent is actually affecting the solubility of diltiazem in the bead. (J.A. Tab 25, A-904.) (Decl of Prof. Roland Bodmeier, Ph.D. in Support of Andrx's Answering Claim Construction Br.) at ¶ 22.) Consequently, unless Biovail obtains an overbroad construction that allows the substitution of the release profile of the diltiazem in place of maintaining the solubility of the diltiazem (the actual claim language), Biovail will not be able to prove infringement by a product that does not meet the limitations of claim 1 in the dry state. Faced with the choice between arguing for a claim construction at odds with the actual claim language, on the one hand, and giving up attempting to enforce a patent that by its very claim language cannot be proven infringed, on the other, Biovail chose the former.

In an effort to support its strained construction, Biovail relies on a heavy-handed edit of a fragment of a sentence found in the prosecution history of the '791 patent. (Biovail Br. at 24-25.) The unedited sentence refers to the control that the wetting agent must have over the solubility of the diltiazem. (J.A. Tab 4, A-51.) Of course, it is this very control that Biovail is seeking to read out of the wetting agent limitation. It is indeed strange that Biovail cites to this sentence in support of a construction that repudiates the clear requirement that the wetting agent actually act to maintain the solubility of the diltiazem in each bead.

Andrx's construction is correct. As demonstrated by a timely General Chemistry textbook, the term "solubility" has a clear and widely understood technical definition: the amount of solid material (expressed in units of mass) capable of being dissolved in a given amount of solvent (expressed in units of volume) to give a saturated solution at a given temperature. (J.A. Tab 11, A-107.) Indeed, this definition is so commonly understood that the inventors did not even bother to mention the word in the specification. The word "maintain" is a commonly used word in the English language that means to keep in existence or continuance, preserve, retain," and "to keep in due condition, operation, or force; keep unimpaired." (J.A. Tab 10, A-104.) Indeed, the inventors used the word "maintain" in the specification consistently with this well-known and understood definition when they stated that they "maintained" a particular dissolution test at "37±0.5°C." (J.A. Tab 1, A-7 at 7:12-13.) The inventors kept the temperature of the test constant, *i.e.,* they maintained that temperature.

Biovail's construction is further erroneous in that Biovail reads the word "solubility" to merely refer to "the condition of being soluble." (Biovail Br. at 23.) Such a construction is at odds with the intrinsic evidence. As Andrx pointed out in its opening brief, any material with a solubility greater than zero is always in a "condition of being soluble," because the chemical compound is capable of being dissolved. (Andrx Br. at 20.) Thus, under Biovail's construction, regardless of whether the wetting agent has any effect at all on the solubility of the diltiazem, the wetting agent would still meet the claim limitation. The prosecution history of the '791 patent sounds a death knell to such a construction:

> In essence, in admixture, the wetting agent appears to control, or strongly influence, the solubility of Diltiazem and does not permit this solubility to be affected by the pH of the gastrointestinal tract. Further, this control appears to occur within the core of diltiazem and wetting agent.
>
> * * *
>
> By combining the wetting agent in admixture with Diltiazem or one or more salts thereof, the solubility of the Diltiazem may be controlled and rendered independent of pH.

(J.A. Tab 5, A-71 – A-72.)

> The wetting agents claimed in the present invention are substances which are believed to modify the solubility of diltiazem inside the coated beads when they are placed in a dissolution medium or when they are ingested by a mammal.

(J.A. Tab 5, A-77.) Similarly, one of the named inventors of the '791 patent declared to the patent office that the presence of the admixture containing wetting agent "is essential to the performance of the final product. . . ." (J.A. Tab 3, A-30.) Under Biovail's proposed construction, none of these representations to the patent office would retain any meaning.

Biovail's suggestion that there is no evidence that the inventors numerically measured the solubility of diltiazem is simply irrelevant. To argue for patentability of their invention, the inventors repeatedly trumpeted the ability of the wetting agent in admixture with diltiazem salt to maintain the solubility of diltiazem. (*See, e.g.*, J.A. Tab 5, A-71 (referring to the ability of the wetting agent to "control or strongly influence" the solubility); A-72 (referring to the ability of the wetting agent to render the solubility of diltiazem "independent of pH").) The inventors chose to include in their claims language regarding maintaining the solubility of the diltiazem. (J.A. Tab 1, A-7 at 8:64-66.) The inventors further chose to require that the solubility of the diltiazem be "unaffected by the pH of the gastrointestinal tract. . . ." (J.A. Tab 1, A-7 – A-8 at 8:66-9:2.) The inventors chose not to include equivocating words in their claim; rather, they clearly claimed that the solubility of the diltiazem must be "unaffected." That is absolute, and that is what the claims should be held to require. Biovail may not now walk away from those critical limitations. The inventors could have sought a patent containing the limitations that

Biovail wishes were included in the '791 patent. They did not. Biovail may not now convert the '791 patent into something the inventors neither sought nor received from the patent office.

Finally, Biovail's reliance on *Applera* is misplaced. (Biovail Br. at 24-25.) In *Applera Corp. v. Micromass UK Ltd.*, 186 F. Supp. 2d 487 (D. Del. 2002), the court construed the term "maintain" to not include variance in a claim limitation that expressly required maintenance "at a relatively low level." *Applera*, 186 F. Supp. 2d at 523-24. The distinction between the claims at issue in *Applera* and those at issue here are evident: the claims at issue in *Applera* explicitly recited the word "***relatively***." Indeed, the *Applera* court specifically pointed to "relatively" in rejecting the argument that maintain means never varying. *Id.* Here, conversely, the patent claims by their very terms require that the solubility be "***unaffected***" by changing pH conditions. (J.A. Tab 1, A-7 at 8:65-67 ("maintain[ing] the solubility . . . ensuring that the solubility of the Diltiazem is ***unaffected*** by the pH of the gastrointestinal tract . . . .") (emphasis added).) Thus, unlike the situation in *Applera*, the claims at issue here contain no wiggle-room qualifiers like "relatively" or "substantially".

The issue here is more similar to the issues presented in *Elantech Devices Corp. v. Synaptics, Inc.*, No. C 06-01839 CRB, 2007 WL 1056782 (Apr. 6, 2007 N.D. Cal.) (Exhibit C hereto) , and in the District Court decision of *Novartis Pharmaceuticals, Inc. v. Eon Labs Mfg., Inc.*, 215 F. Supp. 2d 452 (D. Del. 2002), *aff'd*, 363 F.3d 1306 (Fed. Cir. 2004). In *Elantech*, the court construed the term "maintain" in connection with a patent in accordance with its customary meaning to "continue, retain, or repeat." *Elantech*, at 2007 WL 1056782 at *6. While the invention at issue in *Elantech* was an electromechanical device (a touch screen), the claim limitation, like that at issue here, did not contain any qualifiers to the term "maintaining" as the *Applera* case did. Similarly, the District Court in *Novartis* held that the term "maintaining" in connection with a claim limitation regarding a pharmaceutical composition hydrosol required keeping a variable (in that case, a size distribution) constant. *Novartis*, 215 F. Supp. 2d at 456 (relying on specification statement including word "constant"). The Federal Circuit affirmed that decision, but did not address that particular construction. *Novartis*, 363 F.3d at 1312. Thus,

where, as here, the claims do not contain qualifiers and the intrinsic evidence does not contradict the meaning, it is entirely appropriate to construe "maintain" to require keeping constant, continuing, or retaining.

For these reasons, the Court should adopt Andrx's proposed construction.

**7. The Limitation "ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein" Requires that the Wetting Agent Act to Ensure that the Solubility of the Diltiazem is Unaffected By the pH of the Gastrointestinal Tract or Other Adverse Conditions.**

Here, Biovail, once again, refuses to accept that a composition patent claim must be construed based upon its limitations, not based on what the composition was designed to do ***in the future***. Biovail points to the claim language including the future tense "***will meet***," and argues that "the claim clearly contemplates that the diltiazem ***has already been*** ingested. . . ." (Biovail Br. at 25 (emphasis added.) This argument directly contradicts standard English grammar rules. Read in the context of claim 1 and the accompanying disclosure in the specification, this language demonstrates that the claimed composition already exists before being digested or even ingested. The fact that the claimed composition "will meet" the gastrointestinal tract after ingestion does not mean that the composition did not exist before being ingested. The inventors only disclosed and claimed a dry state composition that "will meet" the gastrointestinal tract and maintain solubility therein. The Court should hold the inventors to what they claimed and disclosed.

**8. The Limitation "said beads being coated with a microporous membrane" Should Be Construed to Require That the Beads are Coated With a Microporous Membrane.**

In a cavalier, two-paragraph blurb, Biovail offers only empty rhetoric and baseless decrees about what it contends is the "plain language" of claim 1. Nowhere does Biovail even attempt to cite ***any*** intrinsic evidence to support its tortured claim construction. Biovail's claim construction fails at every turn.

Even if it were proper (which it is not) to construe the claim language in a vacuum as Biovail has done, the very claim language on which Biovail relies does not support its construction. At bottom, Biovail argues that the claim language "said beads being coated" necessarily means that the "beads have already been coated." The unspoken (and faulty) inference that Biovail does not even bother to articulate is that if "beads have already been coated," then the claimed "beads" necessarily *include* the coating. But contrary to Biovail's interpretation, the claim language treats the claimed "beads" and the microporous coating as separate components of the claimed composition. Had the inventors considered the coating to be part of the claimed "beads," they could easily have claimed beads "including" such a coating. They did not do so, however. This suggests a deliberate choice by the inventors to treat the claimed "beads" independently of the coating.

In any event, when properly construed in light of the rest of the intrinsic evidence (which Biovail ignores entirely), the claimed "beads" do not include the coating. First, as demonstrated in Andrx's opening brief, the inventors in the specification consistently treated "beads" and the coating as different components of the claimed composition;[3] and Biovail's construction would exclude preferred embodiments disclosed in the specification. *See* Andrx Br. at 26-27.

Second, the inventors explained during prosecution that the claimed "beads" are homogeneous. (J.A. Tab 2, A-16 ("the beads produced are homogenous").) A homogenous "bead" that includes an inner spherule of diltiazem and wetting agent surrounded by a discrete coating of water-insoluble polymer and a water soluble or water dispersible polymer – as required by the claims – simply cannot be considered "homogeneous" under any construction of the word. Such a "bead" would by its nature be heterogeneous. This is precisely the same logic

[3] For example, the specification explains that "[s]aid microporous membrane may be applied onto said beads…". (J.A. Tab 1, A-5 at 4:64-65.) This clearly treats the "beads" and the "membrane" as separate components with different antecedent bases.

advanced by the inventors in distinguishing the Debregeas bead from the "bead" claimed in the '791 patent. (J.A. Tab 5, A-74 (emphasis in original).)

Third, as explained above, the inventors ***expressly defined*** "beads" as uncoated:

> each of the independent claims has a separate reference therein to a coating, making it clear that the "beads" are apart from the coating and, in fact, have a coating thereon. ***Thus, the reference to "beads" is to uncoated beads.***

(J.A. Tab 4, A-62-63 (underlined emphasis in original; bold, italic emphasis added).) Thus the inventors' own definition is fatal to Biovail's construction, while fully supporting Andrx's.

For these reasons, this Court should construe the claim term "said beads being coated with a microporous membrane" in accordance with Andrx's construction.

## B. THE '866 PATENT

Biovail's proposed constructions are at odds with the claim language itself and the intrinsic evidence relating to the '866 patent. Indeed, Biovail's proposed constructions appear to be designed not to help define what the claims mean, but rather to broaden the claims to include unknown and undisclosed testing, data-handling, and analysis. Furthermore, Biovail's proposed constructions repudiate the very standards that Biovail specifically incorporated into the claim language and relied upon to generate data that the inventors used to obtain the patent. Consequently, Biovail's open-ended constructions cannot be correct.

### 1. The Limitations "method of United States Pharmacopoeia No. XXIII at 100 RPM in 900 ml of Water" and "method of United States Pharmacopoeia No. XXIII at 100 RPM in 900 ml of the buffered medium" Should Be Construed in Accordance With Andrx's Proposed Constructions.

Biovail complains that Andrx's construction is based on "hand-picking sections of USP 23." (Biovail Br. at 29.) This is simply not true. Any "hand-picking" was done by Biovail and its named inventors long before Andrx had any knowledge of the '866 patent. Andrx's proposed construction merely takes the inventors at their word. The Biovail inventors specified use of United States Pharmacopoeia No. XXIII ("USP 23") in the claims. Examining the specification,

the Biovail inventors specifically defined their invention with reference to testing using Apparatus 1 of USP 23:

> Thus a 24-hour diltiazem preparation is provided wherein the Cmax of diltiazem in the blood is provided from about 10-15 hours after administration of a single dosage to a patient about 9-15 hours after multiple dosages over a number of days ***and displays the dissolution described above determined according to USP 23, page 1791 using Apparatus 1.***

(J.A. Tab 12, A-131 at 12:43-49 (emphasis added).) The inventors went on to directly incorporate the description of Apparatus 1 directly from USP 23 into the specification by a lengthy block quote. (J.A. Tab 12, A-131 – 32 at 12:50 – 13:18.) Significantly, the inventors chose not to block quote Apparatus 2, or any other method from USP 23 in their specification. Similarly, ***every*** figure reporting dissolution testing results in the '866 patent uses Apparatus 1 USP 23 method. (J.A. Tab 12, A-132 at 14:30-14:48.) ***Every*** reported dissolution test on the claimed composition in the body of the specification expressly uses USP 23 Apparatus 1 methods. (*See, e.g.*, J.A. Tab 12, A-133 at 15:60-63; A-134 at 18:6, 18:30, 18:54.) In short, the specification does not describe a ***single*** dissolution test on the claimed composition which uses anything other than Apparatus 1 of USP 23.

Biovail, however, argues despite this clear, unambiguous, and uniform use of Apparatus 1 in USP 23 for all dissolution tests of the claimed compound, that the inventors did not mean to limit their patent to Apparatus 1 of USP 23. Rather, Biovail contends, the inventors meant that any test in accordance with any section or subsection of USP 23 is within the scope of the claims. (Biovail Br. at 28-29.) However, Biovail's various citations to the specification, to the extent they do not refer directly to USP 23, all relate to describing what ***prior art patents*** on ***prior art formulations*** actually reported – not work done by Biovail inventors on formulations described in the '866 patent. (*See, e.g.*, J.A. Tab 12, A-127 at 3:39-49, 3:55-67.) And the remaining citation, which simply parrots the claim language, does not report any dissolution testing results at all. (J.A. Tab 12, A-128 at 5:28-61.) Thus, Biovail's few references to the intrinsic evidence simply do not support its proposed construction.

Biovail also complains that Andrx "adds limitations" relating to the use of "the recited acceptance table" and specifying "a specific UV absorption wavelength." These are not added limitations at all. The very heart of Biovail's claim is that an experiment conducted using USP 23 (Apparatus 1) must fall within certain clearly identified, clearly stated ranges of dissolution.

It would appear that Biovail is arguing that one must conduct an experiment using USP 23 methods, and then abandon the express requirements of that same claimed protocol in order to collect and analyze the data. Biovail cannot be correct. ***First***, the claim itself provides no reference to any other standards for data collection and analysis. ***Second***, every single instance of a dissolution test on the claimed composition in the specification is clear that "the dissolution profiles of all of the strengths were generated from biobatches of capsules using Apparatus 1 (baskets) at 100 RPM in 900 ml of water in accordance with USP 23." (J.A. Tab 12, A-133 at 15:60-63.) ***Third***, if the claim were to allow someone to use only the experimental set-up portion of USP 23, but not require the data collection and analysis to be performed in accordance with the same methods, then the recited dissolution profiles are meaningless. A person of skill in the art would never know whether a particular composition could through some alternative, unspecified data collection and analysis methodology be held to fall within the claimed ranges. Such a construction would violate the fundamental purpose of patent claims: to describe the metes and bounds of a patent's coverage. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005).

Similarly, Biovail's proposed construction is at odds with the *Rhodia* case cited in Andrx's opening brief. (Andrx Br. at 30) (citing *Rhodia Chimie v. PPG Indus. Inc.*, 402 F.3d 1371 (Fed. Cir. 2005)). Under Biovail's construction, ***any*** data handling methodology could be used to compare against the claimed dissolution profile. In *Rhodia*, the Federal Circuit affirmed a claim construction that required the use of a particular standard testing protocol (identified as DIN 53 583) to construe the terms "non-dusting" and "dust free." *Rhodia*, 402 F.3d at 1378. Notably, that particular standard was not included in the claim language itself, but rather appeared only in the specification. *Id.* ("the only measurement of the dust produced by

Examples 5 and 10 was articulated in terms of the DIN 53 583 standard"). Here, the claims specifically call for the application of the USP 23 method, and the only USP 23 dissolution method described in the specification with respect to formulations described is the USP 23 method using Apparatus 1. Moreover, Biovail has not come forward with any evidence (intrinsic ***or*** extrinsic) that the USP 23 Apparatus 2 method would yield the same results as USP 23 Apparatus 1 methods. Because the patent claims would be indefinite if Biovail is allowed to rely on any data-handling and analysis protocol to show infringement, Biovail must be held to its word and the claim should be properly construed to refer to the methods of USP 23, Apparatus 1 and the data-handling and analysis contained therein.

Biovail asserts that Andrx's proposed construction requires the Court to make factual findings as to the "meaning and interpretation of USP 23." (Biovail Br. at 29.) Biovail provides no explanation as to what "factual determinations" Andrx is allegedly asking the Court to make, however. The reason is clear: Andrx's proposed claim construction does ***not*** require the Court to make ***any*** factual determinations. Andrx's proposed construction merely requires the Court to assess the intrinsic evidence and determine what testing is required by the claim language. That is to say, Andrx's proposed construction requires the Court to do exactly what is done by this Court and other courts throughout the United States almost daily during the claim construction process.[4]

Biovail's reliance on *Cybor Corp. v. FAS Technologies, Inc.*, 138 F.3d 1448 (Fed. Cir. 1998), is misplaced.[5] *Cybor*, in relevant part, merely reaffirmed the holding in *Markman* that claim construction is a question of law for the courts, and not a question of fact for the fact-

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[4] Biovail's contention that Andrx's proposed constructions implicate questions of fact is ironic, if not hypocritical. Biovail's opening brief specifically contains a lengthy section entitled "Statement of Facts." (Biovail Br. at 3-9.) Either Biovail is wrong about Andrx's proposed constructions, or Biovail knowingly violated claim construction principles by including an improper "Statement of Facts" in its brief. Biovail cannot have it both ways.

[5] Biovail's citation to *Cybor* in their Opening Claim Construction Brief is incorrect. Andrx has provided the correct citation here.

finder. *Cybor*, 138 F.3d at 1455-56. It is unclear to Andrx why this well-established claim construction principle is even being raised by Biovail here. Certainly Andrx does not challenge the principle that claim construction is a question of law for trial courts, and, since *Biovail* cited *Cybor* for that proposition, apparently neither does *Biovail*.

For these reasons, the Court should construe the claim limitations "method of United States Pharmacopoeia No. XXIII at 100 RPM in 900 ml of Water" and "method of United States Pharmacopoeia No. XXIII at 100 RPM in 900 ml of the buffered medium" in accordance with Andrx's proposed constructions.

**2. The Limitations "higher bioavailability when given at night compared to when given in the morning without food according to FDA guidelines or criteria" and "bioequivalence when given in the morning with or without food according to the same guidelines or criteria" Should Be Construed in Accordance With Andrx's Proposed Constructions.**

Biovail's proposed constructions ignore the specification, and significantly, seek to eschew the requirement that the claimed "higher bioavailability" and "bioequivalence" be assessed "according to FDA guidelines or criteria." In place of these requirements, Biovail contends that two references in the prosecution history, in which the patent office was provided with ratios of two pharmacokinetic parameters in support of an argument relating to higher bioavailability, means that the claim limitation "higher bioavailability" must be read ***solely*** to require those ratios. (Biovail Br. at 31-34.) Biovail appears to argue that the prosecution history trumps ***both*** the claim language ***and*** the specification – the two items entitled to the most attention in claim construction. This cannot be. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1317 (Fed. Cir. 2005) ("because the prosecution history represents an ongoing negotiation between the PTO and the applicant, rather than the final product of that negotiation, it often lacks the clarity of the specification and thus is less useful [than other sources of intrinsic evidence] for claim construction purposes.").

The claim language ***expressly requires*** adoption of the tests set forth in the FDA guidelines and criteria. (J.A. Tab 12, A-137 at 24:13-15.) This express requirement is further

confirmed by the specification, which expressly incorporates by reference those very same guidelines and criteria in their entirety, and block quotes large portions of those guidelines and criteria. (J.A. Tab 12, A-129 – A- 131 at 8:13-12:12.) Significantly, the inventors block-quoted information from these guidelines and criteria which not only address the particular experimental design, but also the proper protocols for collecting and analyzing the data results from those experiments. (*Id.*) The block-quoted passage makes absolutely clear that Andrx's construction requiring use of the 90% confidence interval is correct. (*See, e.g.*, J.A. Tab 12, A-129 at 8:46-47, 8:56-57.) Indeed, the block-quoted passage specifically equates bioavailability and bioequivalence studies. (J.A. Tab 12, A-130 at 10:37-40 ("pharmacokinetic parameters in bioavailability/bioequivalence studies").) Biovail cannot now dodge its express incorporation into the specification and its express recitation of these guidelines and criteria in the claim language.

Biovail's proposed constructions raise more questions than they answer. For example, does the ratio required to assess the "higher bioavailability" limitation require the use of a statistical average for the comparison, or the mean? And if it actually refers to a ratio of the mean values, are those means calculated on a geometric, arithmetic, or log transformed basis? Biovail refuses to say. Only by application of the standards specifically claimed and disclosed guideline and criteria can the '866 patent claims be understood. This situation is similar to the *Rhodia* case, in which the Federal Circuit affirmed a construction which required application of a standard testing protocol discussed in the specification in order to give the claim terms their proper scope. *Rhodia*, 402 F.3d at 1378.

Similarly, Biovail refuses to acknowledge that "bioequivalence" is a term of art that is defined by virtue of standards set forth in FDA guidelines. Biovail incorporated those guidelines by reference into the '866 patent specification, and block-quoted large portion of those guidelines into the specification – including the very 90% confidence interval that Andrx's construction requires. Under the FDA guidelines referred to in the claim and incorporated into the specification, in order for a test sample to be "bioequivalent" the test sample must

demonstrate that the 90% confidence interval[6] falls within 80% - 125% in a head-to-head comparison with a reference sample. Biovail's proposed construction includes none of this required detail. Instead, Biovail simply leaves the door open to question by simply requiring that the composition is "not bioinequivalent." That circular construction begs the question, not bioinequivalent under what test and with reference to what standard?

Ironically, Biovail also complains that Andrx's construction of "higher bioavailability" would require that the claimed composition be "bioinequivalent," whatever that newly-minted word might mean. (Biovail Br. at 33.) Presumably, Biovail means to say that Andrx's construction for "higher bioavailability" requires showing that a claimed composition exceeds the bioequivalence standards when given at night using the claimed FDA guidelines and criteria. If that is what Biovail means, then it is absolutely correct. That is, in fact, what the claims require. The claim expressly recites a "higher bioavailability" in one limitation and "bioequivalence" in a second limitation, and expressly refer to the incorporated FDA guidelines and criteria. (J.A. Tab 12, A-137 at 24:13-18.) The incorporated FDA guidelines and criteria provide critical experimental and data handling information necessary to determine whether compositions are the same (*i.e.*, "bioequivalent") or different under appropriate testing conditions. Since the claim requires "higher bioavailability" between two specified tests, then the claims on their face require that the claimed composition behave differently (using the FDA guidelines and criteria) between the two tests. Because two tests cannot be said to be different if they are "bioequivalent," then Andrx's construction properly requires that the two tests not fall within the scope of bioequivalence as set forth in the FDA guidelines and criteria required by the

[6] The 90% confidence interval is a statistical measure that reports the variability of data collected from a population. In that sense, it is similar to a standard deviation. For example, for data collected from a number of subjects, a mean value might be 25. However, that mean value does not provide any information regarding variation among the subjects. Knowing only the mean, one cannot determine whether each subject tested generated a value of 25, or whether there was a range of experimental values determined. The 90% confidence interval is, therefore, critical under the FDA guidelines for assessing whether two samples are "bioequivalent."

claim language. And since the claim requires not merely that the tests yield different results, but "higher" results, Andrx properly construes the claim to require exceeding the stated bioequivalence standards. In the case of the second limitation, the claim requires "bioequivalence" between two specified tests. That recitation clearly means that the claimed composition must demonstrate bioequivalence in the two tests as set forth in the FDA guidelines and criteria. These constructions are compelled by application of the clear claim language and the specification.

Moreover, Biovail's proposed construction with respect to the meaning of "bioequivalence" is particularly consternating. It proposes reading "bioequivalence" to mean "not bioinequivalent." (Biovail Br. at 33.) In Biovail's view, apparently words can legitimately be defined by adding the word "not" and putting some negative prefix somewhere in the original word. Under Biovail's approach, a claim directed to a "car," for example, would properly be construed to require a "not un-car." That technique merely makes a mockery of the claim construction process.

Finally, Biovail asserts without any statistical evidence that Andrx's proposed construction would not include data from one of the preferred embodiments -- found in Figures 9A and 9B. (Biovail Br. at 33.) Biovail is wrong on the facts and wrong on the law. As set forth in the accompanying declaration of Dr. Sanford Bolton, Andrx's proposed definition of "higher bioavailability" does not exclude the preferred embodiments of Figures 9A and 9B. (J.A. Tab 26, A-976-77.) (Decl. of Sanford M. Bolton, PhD. in Support of Andrx Pharmaceuticals, LLC's and Andrx Corporation's Claim Construction) at ¶¶ 21-24. Moreover, a claim need not encompass every preferred embodiment. *Intamin Ltd. V. Maguetar Technologies*, No. 05-1546, 2007 WL 1138489 at *7 (Fed. Cir. April 18, 2007) (Exhibit D hereto) . Indeed, limitations may be construed to exclude certain embodiments if the prosecution history compels such a result. *North American Container v. Plastipak Packaging*, 413 F.3d 1335, 1346 (Fed. Cir. 2003).

## III. CONCLUSION

For the foregoing reasons, Andrx respectfully requests that the Court construe the disputed limitations of the '791 and '866 patents in accordance with Andrx's proposed constructions.

OF COUNSEL:

Steven Maddox
Jeremy J. Edwards
FOLEY & LARDNER, LLP
3000 K Street, N.W., Suite 500
Washington, DC 20007
Tel: (202) 672-5300

Douglas Carsten
FOLEY & LARDNER, LLP
11250 El Camino Real, Suite 200
San Diego, California 92130
Tel: (858) 847-6700

Martin P. Endres
HEDMAN & COSTIGAN, P.C.
1185 Avenue of the Americas
New York, New York 10036
Tel: (212) 682-7474

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POTTER ANDERSON & CORROON LLP

By: */s/ Kenneth L. Dorsney*
Richard L. Horwitz (#2246)
Kenneth L. Dorsney (#3726)
Hercules Plaza, 6th Floor
1313 N. Market Street
Wilmington, DE 19899
Tel: (302) 984-6000
Fax: (302) 658-1192
rhorwitz@potteranderson.com
kdorsney@potteranderson.com

*Attorneys for Defendants Andrx Pharmaceuticals, LLC and Andrx Corporation*

**IN THE UNITED STATES DISTRICT COURT**
**FOR THE DISTRICT OF DELAWARE**

**CERTIFICATE OF SERVICE**

I, Kenneth L. Dorsney, hereby certify that on April 27, 2007, the attached document was hand-delivered on the following persons and was electronically filed with the Clerk of the Court using CM/ECF which will send notification of such filing(s) to the following and the document is available for viewing and downloading from CM/ECF.

Jack B. Blumenfeld
Karen Jacobs Louden
Morris, Nichols, Arsht & Tunnell
1201 North Market Street
P.O. Box 1347
Wilmington, DE 19899

I hereby certify that on April 27, 2007, I have Electronically Mailed the documents to the following non-registered participants:

Joseph M. O'Malley, Jr.
Preston K. Ratliff, II
Paul, Hastings, Janofsky & Walker LLP
Park Avenue Tower
75 E. 55th Street, First Floor
New York, NY 10022
josephomalley@paulhastings.com
prestonratliff@paulhastings.com

*/s/ Kenneth L. Dorsney*
Richard L. Horwitz
Kenneth L. Dorsney
Potter Anderson & Corroon LLP
Hercules Plaza – Sixth Floor
1313 North Market Street
P.O. Box 951
Wilmington, DE 19899-0951
(302) 984-6000
rhorwitz@potteranderson.com
kdorsney@potteranderson.com

719290